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EXAMINER
HINES, JANA A

ART UNIT	PAPER NUMBER
1645	

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29

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	08/996,768	WENDEL	
	Examiner	Art Unit	
	Ja-Na Hines	1645	

-- The MAILING DATE of this communication appears on the c ver sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 June 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *30-39* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *30-39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Amendment Entry

1. The amendment filed June 7, 2002 has been entered. Claims 30-39 have been newly added. Claims 19-25 and 27-29 are cancelled. Claims 30-39 are under consideration in this office action.

Drawings

2. The drawings have been objected to because of the reasons set forth in the attached PTOL-948. However, the corrections will no longer be held in abeyance and applicant must submit proposed drawing corrections in response to the requirement in the Office action.

Withdrawal of Rejections

3. The following rejections have been withdrawn in view of applicants' amendments:

a) the rejection of claims 19-29 are rejected under 35 U.S.C. 112, second paragraph;

b) the rejection of claims 19-25 and 27-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wendel et al. (EPA 741,294, DE Appl. 19, 516,247), in view of Boyse et al., (US Patent 5,004,681) and;

c) the rejection of claims 19-25 and 27-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wendel et al. (EPA 741,294, DE Appl. 19, 516,247), in view of Dinarello (US Patent 4,434,237) and in further view of Boyse et al., (US Patent 5,192,553).

New Grounds of Rejection

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 30-31 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of determining the presence of a pyrogen in sample of citrated blood comprising contacting a sample of blood with the appropriate reagents and antibodies to detect pyrogens, detecting the presence of pyrogens using an ELISA assay to determine the presence of pyrogens in said sample, does not reasonably provide enablement for method for determining the reaction of blood to test materials and objects for human application comprising a contact step and detecting and/or measuring step. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The specification at pages 10-11 teaches using an ELISA to determine the presence of pyrogens in a blood sample. Figure 1 shows the detection of pyrogens in the cryopreserved blood depending on the amount of pyrogen added. There is no teaching within the specification of any immunofunctional, toxic and/or modulatory reaction being detected and then being used to determine the reaction of blood to the test material. The specification fails to teach examples for determining the reaction to

blood which meets the limitations of the claims or whether the reaction of blood can be in the manner instantly claimed. Therefore, the specification fails to enable a method for determining the reaction of blood to test materials and objects for human application comprising a contact step and detecting and/or measuring step.

Applicants' have provided no guidance to enable one of ordinary skill in the art as to how determine, without undue experimentation, every or any immunofunctional, toxic and/or modulatory reaction being detected; therefore, one of skill in the art would have to locate de novo steps required for a method of determination.

Given the lack of guidance contained in the specification and the unpredictability for a method of determination, one of skill in the art could not make or use the broadly claimed invention without undue experimentation. The specification fails to provide an enabling disclosure for a method of determination, simply comprising a contact and detection step; as there is no step for correlating detection with determination, which could meet the limitations of a method of determination as recited in the claims. In view of the lack of guidance contained in the specification and the unpredictability for the method of determination, one skilled in the art could not make or use the broadly claimed invention without undue experimentation.

5. Claims 30-31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The preamble of the claim 30 is drawn to a method for determining the reaction of blood to test materials and objects for human application. The final step recites a detecting and/or measuring step. There is no step which qualitatively or quantitatively determines what the reaction to the test material is. It is noted that detecting a reaction and determining the type of reaction that the blood has are not equivalent. Thus the preamble is not commensurate in scope with what is being instantly claimed.

Claim 30 is unclear and vague. It is unclear what reaction is being determined. There is no teaching of how to evaluation the blood response upon contact with the material. It is unclear how to determine the reaction of blood.

6. Claim 30 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: The claims lack a correlation step between the related immunofunctional, toxic and/or modulatory reaction to the exposure to test materials and what reaction is being determined. Therefore the claims are rejected.

7. Claims 36-39 are indefinite. The claims recite "in a method of testing..." Because of the phraseology, the claim implies that additional steps are comprised in the method besides the contact and detection step, however the claim does not comprise additional steps. Thus, it is unclear if other method steps are comprised in said method

or only the detection and contact step. Thus, clarification is required to overcome the rejection.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 32-35 are rejected under 35 U.S.C. 102(b) as being anticipated by Boyse et al., (US Patent 5,004,681).

The claims are drawn simply to a blood sample comprising cryopreserved whole blood, wherein the dependant claims further comprise clotting inhibitors and diluents.

Boyse et al., teach the preservation of neonatal or fetal blood cells that have been cryopreserved and thawed can be used for autologous reconstitution. Freezing is destructive to most living cells however cryoprotective agents and optimal cooling rates can protect against cell injury (col. 6 lines 33-46). Various groups have looked at the effect of cooling velocity or cryopreservatives upon the survival or transplantation efficiency of frozen bone marrow cells or red blood cells (col. 6 lines 50-68) and the successful recovery of cells after long-term storage in liquid nitrogen has been described (col. 7 lines 1-17). The blood samples can be received with anticoagulants mixed therein (col. 18 lines 45-48). The collection of blood teaches adding citrate-phosphate-dextrose, as an anticoagulent to the samples (col. 35 lines 32-35). The

inspection and testing of the blood can test for the presence of bacterial cultures (col. 17 lines 40-45) or diagnostic screening for pathogenic microorganisms (col. 17 lines 46-60). Whole neonatal blood cryopreserved and thawed can be used for therapy (col. 24 lines 33-38). Section 6.4 teaches cryopreservation of cord blood stem and progenitor cells derived human blood suspended in various diluents such as RPMI-1640 which are the same diluents added by the instant specification (col. 43-44 lines 35-6).

Therefore, Boyse et al., teach a blood sample comprising cyropreserved units of whole blood comprising clotting inhibitors also known as anticoagulants and diluents just as the instant claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. Claims 30-31 and 36-39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wendel et al. (EPA 741,294, DE Appl. 19, 516,247), in view of Boyse et al., (US Patent 5,192,553). Wendel et al., teach a method for examining substances for pyrogenic activity. The whole blood containing preparations are brought into contact with the substances to be tested and then the preparations are examined for the formation of endogenous pyrogens. The preparations can contain coagulation inhibitors as well as diluents such as cell culture medium or physiological saline. Tests that

measure the formation of the endogenous pyrogens include measurements of interleukin-1, interleukin-6, tumor necrosis factor, or PGE_2. However, Wendel et al., is silent to the use a sample of thawed cryopreserved whole blood in the method.

Boyse et al., has been discussed above and teach the use of thawed cryopreserved whole blood in testing methods.

It would have been prima facie obvious to have modify the method of determination of the reaction of blood or the detection of a blood reaction as taught by Wendel et al., wherein the modification includes using cryopreserved whole blood as taught by Boyse et al. One would have a reasonable expectation of success in using cyropreserved blood samples as taught by Boyse et al., (5,004,681) in the method of Wendel et al., because cyropreserved blood does not lose its ability to function and cryopreservation can be stored until use. Moreover, the use of cryopreserved blood comprising diluents and clotting inhibitors provides advantages in the method of Wendel et al., wherein the blood can be stored until its ready for testing.

Response to Arguments

10. Applicant's arguments filed June 7, 2002 have been fully considered but they are not persuasive.

In response to applicant's argument that there is no suggestion to combine the references, because an allegation of functional equivalents does not establish motivation to demonstrate obviousness under section 103(a), the examiner recognizes that obviousness can only be established by combining or modifying the teachings of

the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, Wendel et al., teach the method of determination of the reaction of blood or the detection of a blood reaction as taught by Wendel et al., and Boyse et al., teach inspection and testing of the blood can test for the presence of bacterial cultures or diagnostic screening for pathogenic microorganisms. No more than routine would have been required to use a croypreserved whole blood sample in the method since such blood samples maintained their ability to function, can be cryopreserved and stored until use while comprising diluents and clotting inhibitors, and the prior art teaches that no more than routine skill is required to create a cryopreserved sample using well known and commercially available reagents.

Conclusion

11. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any

extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ja-Na Hines whose telephone number is (703) 305-0487. The examiner can normally be reached on Monday through Thursday from 6:30am to 4:00pm. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached on (703) 308-3909. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Ja-Na Hines

January 13, 2003

LYNETTE R. F. SMITH
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER